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(54) Title: NEOPLASM SPECIFIC ANTIBODIES AND USES THEREOF

(57) Abstract: The present invention features polypeptides, such as antibodies, and their use in the treatment and diagnosis of neoplasms.

AMENDED CLAIMS

[received by the International Bureau on 27 December 2004 (27.12.04); original claims 1, 10, 11 and 15-50 amended; claims 16 and 17 cancelled; remaining claims unchanged (7 pages)]

Amended Claims 1 to 50

1. A purified polypeptide that specifically binds to a neoplastic cell, but does not bind to a non-neoplastic cell, wherein said purified polypeptide specifically binds to a diffuse-type stomach adenocarcinoma, an intestinal-type stomach adenocarcinoma, an adenocarcinoma of the colon, an adenocarcinoma of the lung, a squamous cell carcinoma of the lung, a squamous cell carcinoma of the esophagus, an adenocarcinoma of the pancreas, a urothel carcinoma of the urinary bladder, a renal cell carcinoma of the kidney, an adenocarcinoma of the prostate, an invasive ductal carcinoma of the breast, an invasive lobular carcinoma of the breast, an adenocarcinoma of the ovary, and an adenocarcinoma of the uterus, and not to non-neoplastic cells of the same tissue type, and wherein said purified polypeptide is at least 90% identical to the full-length sequence of SEQ ID NO:2.
2. The purified polypeptide of claim 1, wherein said polypeptide specifically binds to at least one of lung adenocarcinoma cell line Colo-699 (DSMZ accession number ACC 196), lung adenocarcinoma cell line DV-90 (DSMZ accession number ACC 307), epidermoid lung carcinoma cell line EPLC-272H (DSMZ accession number ACC 383) or lung squamous cell carcinoma cell line LOU-NH91 (DSMZ accession number ACC 393).
3. The purified polypeptide of claim 1, wherein said polypeptide induces apoptosis of said neoplastic cell, but does not induce apoptosis of said non-neoplastic cell.
4. The purified polypeptide of claim 1, wherein said polypeptide decreases proliferation of said neoplastic cell, but does not decrease proliferation of said non-neoplastic cell.
5. A purified polypeptide comprising the amino acid sequence of SEQ ID NO:2.

6. A purified polypeptide comprising amino acids 16-22, 37-52, and 85-103 of SEQ ID NO:2.

7. The purified polypeptide of claim 5 or 6, wherein said purified polypeptide specifically binds to a diffuse-type stomach adenocarcinoma, an intestinal-type stomach adenocarcinoma, an adenocarcinoma of the colon, an adenocarcinoma of the lung, a squamous cell carcinoma of the lung, a squamous cell carcinoma of the esophagus, an adenocarcinoma of the pancreas, a urothelial carcinoma of the urinary bladder, a renal cell carcinoma of the kidney, an adenocarcinoma of the prostate, an invasive ductal carcinoma of the breast, an invasive lobular carcinoma of the breast, an adenocarcinoma of the ovary, and an adenocarcinoma of the uterus, and not to non-neoplastic cells of the same tissue type.

8. The purified polypeptide of any one of claims 1-6 wherein said polypeptide is an antibody or a functional fragment thereof.

9. The purified polypeptide of claim 8, wherein said antibody is a monoclonal antibody or a functional fragment thereof.

10. The purified polypeptide of claim 8, wherein said functional fragment is selected from the group consisting of V_{H} , Fab, Fab', and F(ab')₂.

11. The antibody produced by the LM-1 cell line having DSMZ Deposit Accession No. DSM ACC2623.

12. A functional fragment of an antibody, wherein said functional fragment comprises amino acids 16-22, 37-52, and 85-103 of SEQ ID NO:2.

13. The functional fragment of claim 12, wherein said functional fragment is a functional fragment of a monoclonal antibody.

14. The functional fragment of claim 12, wherein said functional fragment is a V_H chain of an antibody.

15. A purified polypeptide that specifically binds an antibody, or functional fragment thereof, comprising the sequence of SEQ ID NO:2, wherein said polypeptide has an apparent molecular weight of approximately 70 kDa using sodium dodecyl sulfate polyacrylamide gel electrophoresis and, wherein said purified polypeptide is a polypeptide expressed by lung adenocarcinoma cell line Colo-699 (DSMZ accession number ACC 196), lung adenocarcinoma cell line DV-90 (DSMZ accession number ACC 307), epidermoid lung carcinoma cell line EPLC-272H (DSMZ accession number ACC 383) or lung squamous cell carcinoma cell line LOU-NH91 (DSMZ accession number ACC 393), but said polypeptide is not expressed by non-neoplastic cells of the same tissue type.

16. The purified polypeptide of claim 15, wherein said polypeptide, if present on a cell and bound by said antibody or functional fragment thereof, results in apoptosis of said cell.

17. The purified polypeptide of claim 15, wherein said polypeptide, if present on a cell and bound by said antibody or functional fragment thereof, results in a reduction in proliferation of said cell.

18. An isolated nucleic acid molecule encoding the amino acid sequence of SEQ ID NO:2.

19. An isolated nucleic acid molecule comprising nucleic acids 46-66, 109-156, and 253-309 of SEQ ID NO:1.

20. A vector comprising the nucleic acid molecule of claim 20 or 21.

21. An isolated cell comprising the vector of claim 22.

22. An isolated cell that expresses the polypeptide of any one of claims 1-10.

23. The isolated cell of claim 24, wherein said isolated cell is a mammalian cell.

24. The isolated cell of claim 25, wherein said mammalian cell is a human cell.

25. The isolated cell of claim 24, wherein said polypeptide is an antibody.

26. The isolated cell of claim 27, wherein said antibody is an IgM antibody.

27. The isolated cell of claim 24, wherein said antibody is a monoclonal antibody.

28. A method of producing the purified polypeptide of any one of claims 1-10, said method comprising contacting a cell with the vector of claim 22 and isolating the polypeptide expressed by said cell.

29. Use of the purified polypeptide of any one of claims 1-10 in a method of diagnosing a neoplasm in a mammal, said method comprising the steps of, (a) contacting a cell or tissue sample derived from said mammal with the purified polypeptide of any one of claims 1-10, and (b) detecting whether said purified polypeptide binds to said cell or tissue sample, wherein binding of said purified polypeptide to said cell or tissue sample is indicative of said mammal having a neoplasm.

30. The use of claim 31, wherein said cell or tissue is derived from a stomach, a colon, a lung, an esophagus, a pancreas, a urinary bladder, a kidney, a prostate, a female breast, an ovary, or a uterus.
31. The use of claim 31, wherein said mammal is a human.
32. The use of claim 31, wherein said polypeptide is an antibody.
33. The use of claim 34, wherein said antibody is a monoclonal antibody.
34. The use of claim 31, wherein said polypeptide is conjugated to a detectable agent selected from the group consisting of a radionuclide, a fluorescent marker, an enzyme, a cytotoxin, a cytokine, and a growth inhibitor.
35. The use of claim 36, wherein said detectable agent is capable of inducing apoptosis of said cell.
36. The use of claim 31, wherein said polypeptide is conjugated to a protein purification tag.
37. The use of claim 38, wherein said protein purification tag is cleavable.
38. Use of the purified polypeptide of any one of claims 1-10 in a method of treating a proliferative disorder in a mammal, said method comprising the step of contacting a cell with the purified polypeptide of any one of claims 1-10, wherein binding of said purified polypeptide to said cell results in a reduction in proliferation of said cell.

39. The use of claim 40, wherein said proliferative disorder is a diffuse-type stomach adenocarcinoma, an adenocarcinoma of the colon, an adenocarcinoma of the lung, a squamous cell carcinoma of the lung, a squamous cell carcinoma of the esophagus, an adenocarcinoma of the pancreas, a urothelial carcinoma of the urinary bladder, a renal cell carcinoma of the kidney, an adenocarcinoma of the prostate, an invasive ductal carcinoma of the breast, an invasive lobular carcinoma of the breast, an adenocarcinoma of the ovary, or an adenocarcinoma of the uterus.

40. The use of claim 40, wherein said mammal is a human.

41. The use of claim 40, wherein said polypeptide is an antibody.

42. The use of claim 43, wherein said antibody is a monoclonal antibody.

43. The use of claim 40, wherein said polypeptide is conjugated to a detectable agent selected from the group consisting of a radionuclide, a fluorescent marker, an enzyme, a cytotoxin, a cytokine, and a growth inhibitor.

44. The use of claim 45, wherein said detectable agent is capable of inhibiting cell proliferation of said cell.

45. The use of claim 40, wherein said polypeptide is conjugated to a protein purification tag.

46. The use of claim 47, wherein said protein purification tag is cleavable.

47. A medicament comprising the purified polypeptide of any one of claims 1-10 in a pharmaceutically acceptable carrier.

48. A diagnostic agent comprising the purified polypeptide of any one of claims 1-10.

49. A purified antibody or functional fragment thereof, wherein said antibody or functional fragment specifically binds a polypeptide having an apparent molecular weight of approximately 70 kDa using sodium dodecyl sulfate polyacrylamide gel electrophoresis and, wherein said polypeptide is a polypeptide expressed by lung adenocarcinoma cell line Colo-699 (DSMZ accession number ACC 196), lung adenocarcinoma cell line DV-90 (DSMZ accession number ACC 307), epidermoid lung carcinoma cell line EPLC-272H (DSMZ accession number ACC 383) or lung squamous cell carcinoma cell line LOU-NH91 (DSMZ accession number ACC 393), but not by non-neoplastic cells of the same tissue type.

50. The cell line having DSMZ Deposit Accession No. DSM ACC2623.